

RemarksApplication Status and Disposition of Claims

Claims 1-3, 6-31, and 34 are pending. Claims 1-3, 6-18, 30 and 31 are under consideration. Claims 19-29 and 34 have been withdrawn from consideration as directed to a non-elected invention.

Applicants note that the withdrawn claims are kept pending, subject to possible rejoinder.

Statement of Interview

Applicants express appreciation for the courtesies extended by Examiner Popa during an April 12, 2011 interview with Applicants' representative Walter Schlapkohl. During the interview, Applicants representative distinguished the claimed subject matter from the art cited art in the Office Action dated February 4, 2011. For example, Applicants' representative indicated that the obviousness rejections of record failed to make a *prima facie* case under 35 U.S.C. § 103 at least because the Office did not appear to be considering the art as a whole. In particular, Applicants' representative asserted that the high capture rate of leukocytes in, for example, Oka et al. (U.S. Patent No. 5,298,165, hereinafter "OKA 1"), suggests that the leukocytes are bound tightly to the filter such that one of ordinary skill in the art would not expect to achieve a high recovery rate of the leukocytes in the event that the filter were washed.

The Examiner was not initially persuaded by the remarks presented during the interview, and no agreement was reached. However, the Examiner indicated that she remained open to further consideration of remarks and/or evidence which may distinguish the claimed subject matter from the cited art, including any remarks and/or evidence relating to the recovery and recovery rate of nucleated cells achieved by the present invention.

Claim Rejections – Obviousness-Type Double Patenting

The Office Action maintains the rejection of claims 1-3, 6-18, 30 and 31 on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1, 6, and 12-

17 of U.S. Patent No. 6,268,119 (hereinafter "SUMITA") in view of OKA 1, Oka et al. (U.S. Patent Application Publication No. 2004/0251195, hereinafter "OKA 2"), Fukuda et al. (WO 02/087660, hereinafter "FUKUDA"), and Rubenstein et al. (*Proc. Nat'l Acad. Sci. USA*, 1995, **92**:10119-10112, hereinafter "RUBENSTEIN").

Applicants respectfully disagree with the Office for the reasons set forth previously in prior responses. For brevity, the content of those responses is not restated here, but is expressly incorporated by reference as though set forth in full herein. Applicants maintain that the Examiner's rejection is legally incorrect and request its withdrawal.

In addition, Applicants submit on even date herewith a Declaration under 37 C.F.R. § 1.132 by Dr. Mikitomo YASUTAKE, a joint inventor of the claimed subject matter. In particular, Applicants submit that the Declaration supports the previous and instant remarks with respect to the claimed subject matter and its nonobviousness over claims 1, 6, and 12-17 of SUMITA in view of OKA 1, FUKUDA, OKA 2, and RUBENSTEIN. However, Applicants note that the Declaration is not limited to a discussion of the cited claims in SUMITA and should not be construed as limited to the non-obviousness of the claimed subject matter over the *claims* of SUMITA (see further Remarks regarding the YASUTAKE Declaration with regard to the obviousness rejection under 35 U.S.C. § 103(a), below).

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the non-statutory obviousness-type double patenting rejection.

Claim Rejections – 35 U.S.C. § 103

The Office Action maintains the rejection of claims 1-3, 6-17, 30 and 31 under 35 U.S.C. § 103(a) as being obvious over SUMITA in view of OKA 1, FUKUDA, OKA 2, and RUBENSTEIN.

Applicants respectfully disagree with the basis for the rejections as set forth in the prior responses, which reasons for disagreement are not restated here, but are expressly incorporated by reference as though set forth in full herein. Applicants also submit that claims 1-3, 6-17, 30

and 31 are not obvious over SUMITA in view of OKA 1, FUKUDA, OKA 2, and RUBENSTEIN for at least the following reasons.

Declaration by Dr. Mikitomo YASUTAKE

Applicants submit on even date herewith a Declaration under 37 C.F.R. § 1.132 by Dr. Mikitomo YASUTAKE, a joint inventor of the claimed subject matter. In particular, Applicants submit that the Declaration supports the previous and instant remarks with respect to the claimed subject matter and its nonobviousness over the cited art. Applicants further note that “[w]hen an applicant timely submits evidence traversing a rejection, the examiner must reconsider the patentability of the claimed invention” and that such reconsideration “must be based on consideration of the *entire record*, by a preponderance of the evidence, with due consideration to the persuasiveness of any arguments and any secondary evidence. *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992)” (MPEP 716.01(d); emphasis added). Thus, Applicants respectfully request that the Examiner reconsider the claimed subject matter in view of all of the arguments previously set forth in the record, the arguments which follow, as well as in view of the attached Declaration.

The Rejection Fails to Consider the Invention or the Cited Art as a Whole

In addition to the reasons set forth in the attached Declaration, Applicants submit that the rejection under 35 U.S.C. § 103(a) over SUMITA in view of OKA 1, FUKUDA, OKA 2, and RUBENSTEIN fails to set forth a *prima facie* case of obviousness at least because the rejection fails to consider the claimed invention and the cited art *as a whole*. MPEP 2141.02 states that “[a]scertaining the differences between the prior art and the claims at issue requires interpreting the claim language, and considering both the invention and the prior art references *as a whole*” (emphasis added). In this regard, the obviousness rejection in the Office Action dated February 4, 2011 is deficient because it appears to rely on an improper “picking and choosing” of diverse teachings of structural filter features and method steps from five separate documents rather than a consideration the cited art (or the invention) as a whole. The result is a misplaced focus on each separate structural feature and/or method step. This misplaced focus improperly limits the

Office's consideration of Applicants' invention to a mere combination of parts rather than a novel method of monocyte *recovery*.

For example, the rejection appears to rely on SUMITA for disclosure of a general method of preparing a nucleated cell concentrate that includes introducing blood into a filter device which captures nucleated cells and discharges unnecessary cells (Office Action at page 8, 2nd paragraph). The rejection asserts that the SUMITA elutes the nucleated cells by introducing a recovery solution into the filter device. *Id.* The rejection further asserts that the unnecessary cells of SUMITA are erythrocytes and that the recovery solution could be plasma. The rejection then jumps to a consideration of OKA 1, relying on OKA 1 for structural features associated with the filter system (Office Action at paragraph bridging pages 8 and 9). The rejection then asserts that one of skill in the art would have been motivated to use the filter system of OKA 1 in the method of SUMITA because "composite filters are very efficient in *removing* nucleated cells from blood" and "because the art teaches that composite filters can be successfully used to *capture* blood nucleated cells" (page 9, emphasis added). In so doing, the rejection appears to disregard recited features of Applicants' claimed subject matter. For example, claim 1 is directed, *inter alia*, to *recovery* of nucleated cells captured a filter material. Claim 1 is further directed, *inter alia*, to a method for preparing a cell concentrate which includes (1) introduction of a layer of unnecessary cells into a filter device followed by (2) introduction of a layer of nucleated cells into a filter device such that unnecessary cells are discharged and nucleated cells remain. (The recovery of the nucleated cells occurs *after* the nucleated cells have been captured in the filter material.)

In contrast, OKA 1 is directed to a two-stage method of leukocyte *removal* (paragraph bridging columns 6-7; claim 1). In the first stage, a blood product is filtered to remove at least 60% of all leukocytes. *Id.* In the second stage, the leukocyte-depleted blood product is subjected to a second treatment by passing through a microfilter element comprised of a non-woven or a woven fabric having a small average fiber diameter. *Id.* Further, SUMITA is directed to the use of a *recovery liquid having definite viscosity* (not introduction of separate cell layers) to solve the problem of separating and recovering necessary cells (see SUMITA, e.g., at column 2, lines 37-42). Thus, even when considered in combination, SUMITA and OKA 1 fail to render obvious

the claimed method of recovering nucleated cells which includes, *inter alia*, (1) introduction of a layer of unnecessary cells into a filter device followed by (2) introduction of a layer of nucleated cells into the filter device such that unnecessary cells are discharged and nucleated cells remain.

Indeed, Applicants submit that OKA 1 teaches away from the instantly claimed subject matter at least because, when considered as a whole, OKA 1 suggests that leukocytes are bound tightly to the filter such that one of ordinary skill in the art would not expect to achieve a high recovery rate of the leukocytes in the event that the filter were washed. In this regard, OKA 1 is directed to a method of *removing leukocytes* and *recovering red blood (unnucleated) cells* from a leukocyte-containing blood product to prepare leukocyte-free blood for transfusions (see, e.g., Abstract; column 1, lines 17-27; and paragraph bridging columns 21 and 22). Thus, one of ordinary skill in the art would understand that OKA 1 was not concerned with subsequent recovery of the leukocytes. Moreover, one of ordinary skill in the art would understand that OKA 1 suggests that tight binding of leukocytes to the filter of OKA 1 would not result in a high recovery rate of nucleated cells.

FUKUDA and OKA 2, like OKA 1, are related to elimination of leukocytes. The rejection fails to address this point, however, and instead asserts that both FUKUDA and OKA 2 disclose a method of centrifuging blood prior to filtration, which method is alleged to “necessarily result in a cell gradient comprising a buffy coat at the top, (layer rich in nucleated cells), plasma in the middle (nucleated cell-diluted layer), and an erythrocyte pellet at the bottom (layer rich in unnecessary cells) with the introduction into the filter of the separated components in the order of erythrocyte pellet first, plasma second, and buffy coat third” (Office Action at page 10, bottom). Again, this focus on one aspect of FUKUDA and/or OKA 2 fails to consider these documents *as a whole*. Moreover, the approach set forth by the Office improperly assumes that Applicants’ claimed subject matter may be deconstructed to a mere series of parts. FUKUDA and OKA 2, like SUMITA and OKA 1, fail to teach or suggest the present invention, which invention, *inter alia*, recovers nucleated cells at an increased rate not taught by the combination of cited documents.

Indeed, as argued previously, Applicants respectfully submit that unexpected results observed with the present invention weigh in favor of nonobviousness. As demonstrated in Examples 1 and 2 and in Comparative Example 1 of the specification, the volume of erythrocytes can be reduced and mononuclear cell recovery rate increased by first introducing the layer rich in unnecessary cells into a filter and then introducing the layer rich in nucleated cells into the filter. As noted above, because OKA 1, OKA 2, and FUKUDA are not concerned with nucleated cell recovery, they provide no suggestion at all about the increased recovery achieved by the specifically recited steps of the present invention. Applicants respectfully submit that the unexpected results obtained cannot have been predicted based on the teachings of OKA 1, OKA 2, FUKUDA, and SUMITA.

With regard to RUBENSTEIN, the rejection appears to rely on RUBENSTEIN for alleged disclosure of adding HES to blood to enhance erythrocyte sedimentation (Office Action at page 11, lines 10-11). Applicants submit that RUBENSTEIN fails to compensate for the deficiencies of the other cited documents discussed above.

Based at least on the foregoing, Applicants submit that the claimed subject matter is not obvious over SUMITA in view of OKA 1, FUKUDA, OKA 2, and RUBENSTEIN. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

The Office Action also rejects claims 1-3, 6-18, 30 and 31 under 35 U.S.C. § 103(a) as being obvious over SUMITA in view of OKA 1, OKA 2, FUKUDA, RUBENSTEIN, and further in view of Tanaka et al. (U.S. Patent No. 6,048,464, hereinafter "TANAKA").

In response, Applicants submit that claims 1-3, 6-18, 30 and 31 are not obvious over SUMITA in view of OKA 1, OKA 2, FUKUDA, RUBENSTEIN, and/or TANAKA for at least the reasons set forth above. In particular, Applicants submit that TANAKA

fails to compensate for the deficiencies of SUMITA, OKA 1, OKA 2, FUKUDA, and/or RUBENSTEIN.

Based at least on the foregoing, Applicants submit that the claimed subject matter is not obvious over SUMITA in view of OKA 1, OKA 2, FUKUDA, RUBENSTEIN, and TANAKA. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

Conclusion

In view of the foregoing remarks and amendments, Applicants respectfully request withdrawal of the rejections set forth in the Office Action of February 4, 2011.

Applicants hereby authorize the charging of any required fees necessary for consideration of this paper to Deposit Account No. 19-0089. Any comments or questions concerning this application can be directed to the undersigned at the telephone number given below.

Respectfully submitted,
Shuji TERASHIMA et al.

/Walter Schlapkohl/
Reg. No. 64,416
Walter Schlapkohl

Bruce H. Bernstein
Reg. No. 29,027

August 4, 2011
GREENBLUM & BERNSTEIN, P.L.C.
1950 Roland Clarke Place
Reston, VA 20191
(703) 716-1191